

## **Remarks**

### **Status of the Application**

Claims 68-72 and 74-87 are pending with the entry of this amendment. Claims 68-72, 74-76 and 78-80 stand rejected under 35 U.S.C. § 102(e). Claims 71, 76 and 81 stand rejected under 35 USC § 103(a). Claim 77 is objected to as being dependent upon a rejected base claim, but the Examiner has kindly indicated that this claim would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

### **Amendments to the Claims**

Please amend claims 68 and 77 as indicated above, and please add new claims 82-87. These amendments and new claims introduce no new matter and support for the amendments is replete throughout the application as originally filed. Support for the amendment to claim 68, and for new claims 83-87 is found in the specification at, for example, page 6 lines 5-7 ("In one embodiment of the invention, the capillary 125 is connected to a high pressure liquid chromatography source that provides the HPLC liquid."). Support for new claim 82 is found in the specification at, for example, page 6, lines 25-27 ("The droplet may have a controlled, adjustable size or volume, depending upon flow-rate through the capillary . . .").

These amendments are made without prejudice and are not to be construed as abandonment of the previously claimed subject matter, or agreement with any objection or rejection of record.

### **The 35 U.S.C. § 102(e) Rejection**

Claims 68-72, 74-76 and 78-80 stand rejected under 35 U.S.C. § 102(e) as allegedly being unpatentable over O'Connor *et al.*, US 2002/0003177 ("O'Connor"). Applicants respond by amendment in part and traverse in part.

Applicants have amended claim 68 to recite that the claimed sample deposition system includes "a high pressure liquid chromatography (HPLC) source in fluid communication with the capillaries, which HPLC source causes a liquid to flow through and form a droplet at an end of each capillary." The apparatus described in the O'Connor reference does not include an HPLC source, or any other type of pump that causes liquid to flow. In fact, O'Connor teaches

away from the use of pumps such as HPLC sources. For example, in describing the background art, O'Connor states that:

“[p]ositive displacement jetting comes in many forms and is the oldest method of droplet formation. Pumps and valves are used to produce displacement of fluid at a tip orifice. . . . These methods for dispensing liquids involve either a complicated valving system (for positive displacement, eg) or have an active jet head (either piezo jet, thermal jet, or capillary spotting). *The former [pumps] cannot make small drops.*” (paragraphs 0009 and 0011, emphasis added).

O'Connor does not anticipate Applicants' claimed invention for at least one additional, independent reason. Claim 68 recites that the liquid dispensed by claimed apparatus *flows through the capillary* to form a droplet at an end of a capillary before application of the electric field (this claim element is present in claim 68 both as currently amended and as previously presented). In marked contrast, the liquid dispensed by the O'Connor apparatus does not flow through the capillary prior to application of the electric field. In contrast, O'Connor states that the liquid does not flow until after the electric field is applied (see, e.g., O'Connor, paragraph 0045, “the liquid [in the dispensing tip] is under sufficient hydrostatic pressure to prime the line, but not sufficient to overcome the surface tension forces of the meniscus at the bottom of the tip, *and therefore liquid normally does not flow.* This meta-stable state is disrupted when a voltage pulse is generated by the voltage generator (23) and applied to the liquid within the dispensing head causing a charge differential to occur at the liquid-to-air interface.” (emphasis added).

O'Connor therefore does not describe each element of claim 68, so this claim is not anticipated by O'Connor. Claim 69-72, 74-76 and 78-80, each of which depends from claim 68, necessarily are likewise not anticipated by O'Connor. Moreover, since O'Connor teaches away from at least two elements of Applicants' claims (having an HPLC source connected to the capillary, and causing the liquid to flow through the capillary prior to application of the electric field), these claims are not obvious over O'Connor.

#### **The 35 U.S.C. § 103(a) Rejections**

Claim 71 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over O'Connor. This claim, which is directed to a sample deposition system that includes a motion

table upon which one or more sample holders are placed, depends from claim 68. As discussed above, at least two elements of claim 68 are not described in O'Connor. In particular, O'Connor does not teach or suggest a sample deposition system such as that claimed by Applicants, which has an HPLC source connected to a capillary, and requires liquid to flow through the capillary prior to application of the electric field. Therefore, claim 71 is not *prima facie* obviousness over O'Connor.

Claim 76 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over O'Connor in view of Morozova *et al.* (*Anal. Chem.* 71: 3110-3117 (1999)). As discussed above, at least two elements of claim 68, from which claim 76 depends, are not suggested by O'Connor. The Morozova reference does not suggest these claim elements for which teachings are lacking in O'Connor. In fact, Morozova teaches away from the use of a pump to feed liquid, stating that "[t]he trouble with use of the pump is that occasional droplets are ejected from the ES [electrospray] capillary upon any instability of the ES, e.g., upon the passage of a small dust particle through the tip. Subsequently, we abandoned the pump in favor of a free capillary, where the delivery of solution is automatically regulated by the spray itself." (page 3112, column 1, paragraph 4). Therefore, claim 76 is not obvious over O'Connor in view of Morozova.

Claim 81 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over O'Connor in view of Sauter *et al.* (US 6,149,815). This claim is directed to a sample deposition system in which the capillaries are connected to a liquid chromatography system. As discussed above, O'Connor teaches away from Applicants' claimed sample deposition system that includes an HPLC source connected to a capillary. Sauter also teaches away from the use of any type of pump, stating that "[d]evices that employ pneumatic, peristaltic or other pumps cannot address the dynamic range of such a device (in fact they cannot dispense nanoliters with high accuracy and precision), and they require complex pumping and robotic systems to execute such functions if they attempt true parallel operation at all." (Column 11, lines 21-27). The device described by Sauter is similar to that described by O'Connor in that both devices rely on surface tension and capillary action to maintain the liquid in the capillary, in a steady (non-flowing) state, until the electric field is applied. Thus, neither of these cited references teaches or suggests a deposition system such as that claimed by Applicants in which the liquid flows through the capillary to form a droplet prior to application of the electric field. Therefore, since independent claim 68 is not

obvious over the cited references, dependent claim 81 is likewise not obvious over these references.

### **The Objection to Claim 77**

The Examiner has indicated that claim 77 would be allowable if amended to incorporate all of the limitations of the rejected base claim. Although Applicants have amended and/or traversed the rejections of the base claim 68, Applicants also have amended claim 77 to incorporate all of the limitations of claim 68. The amendment of claim 77 is not intended as an acquiescence to the rejection of the base claims, but rather is merely to expedite prosecution.

### **The New Claims**

Applicants have added new claims 82-87. These claims are not anticipated by, or obvious over, any of the cited references. In particular, claim 82, which depends from claim 68, recites that the flow rate through a capillary regulates the size of the liquid droplet. O'Connor and Sauter teach away from this claim element, stating as discussed above that the liquid does not flow through the capillaries before application of the electric field.

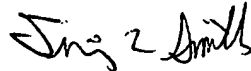
Independent claim 83 is directed to a sample deposition system that includes an HPLC source that causes a liquid to flow through, and form a droplet at an end of, a capillary. These claim elements are not described by O'Connor or Sauter, as discussed above with respect to claim 68. In fact, these references teach away from a system having an HPLC source or other type of pump. Therefore, although claim 83 does not include claim limitations that were previously added to claim 68 to overcome a rejection based on Sauter and King (US 6,132,582) (i.e., that the electric field is formed by applying a charge to the sample plate and a ground to the liquid droplet), claim 83 is nevertheless not anticipated by, or obvious over, any of O'Connor, Sauter, or King, taken alone or in combination. New claims 84-87 depend from claim 83, and therefore are likewise patentable over the cited references.

Applicants have cited Ohno (US 3,941,312) in an information disclosure statement submitted concurrently with this amendment. The arguments made above with respect to O'Connor, Morozova, King and Sauter apply also to Ohno. In particular, Ohno does not describe a sample deposition system such as that claimed by Applicants which has an HPLC chromatography source, or in which a liquid flows through a capillary prior to application of the electric field.

**Conclusion**

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for examination. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned attorney at 858-812-1547.

Respectfully submitted,



Timothy L. Smith, Ph.D.  
Reg. No. 35,367

GENOMICS INSTITUTE OF THE NOVARTIS RESEARCH FOUNDATION  
10675 John Jay Hopkins Drive, Suite E225  
San Diego, CA 92121  
Tel: (858) 812-1547  
Fax: (858) 812-1981